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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/869,386	06/05/97	SASTRY J	UTXC:538/HYL

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EXAMINER	
NELSON, B	
ART UNIT	**PAPER NUMBER**
1648	12

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/869,386	Applicant(s) Sastry, et al.
	Examiner Brett Nelson	Group Art Unit 1648

☒ Responsive to communication(s) filed on *Feb 16, 1999* .

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *29-47* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *29-47* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior office action.

2. The examiner acknowledges receipt of the Request for Reconsideration filed Feb. 16, 1999. Claims 29-47 are pending and under consideration.

3. The previous rejection under 35 U.S.C. 112, first and second paragraphs, are withdrawn in view of applicant's arguments.

Specification

4. The application is objected to because of alterations which have not been initialed and/or dated as is required by 37 CFR 1.52(c). A properly executed oath or declaration which complies with 37 CFR 1.67(a) and identifies the application by application number and filing date is required.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

5. Claims 29-47 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting HIV entry into a cell *in vitro* comprising contacting the cell with peptides consisting of SEQ ID NOs: 1, 3, or 5, does not reasonably

provide enablement for a method of inhibiting HIV entry into a cell *in vivo* employing all of the possible claimed peptide sequences. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The claims are drawn to a method of directly inhibiting HIV entry into a cell comprising contacting the cell with a composition comprising a peptide of 8-24 residues comprising SEQ ID NO:5. The specification at pages 65-67 and Fig. No. 8 disclose culturing MT-4 cells and primary human T cells in the presence of HIV and a selected peptide from the V3 loop of gp120 and the reverse transcriptase assays showed a decrease in the amount of reverse transcriptase produced in the cells incubated with certain peptides. However, the specification does not show a correlation between that which occurred *in vitro* to that which one of skill in the art would reasonably expect *in vivo*.

The specification provides no probative evidence to support the claimed treatment which would protect humans against HIV infection. The obstacles to treatment development and therapeutic approaches with regard to retroviruses associated with AIDS in humans are well documented in the literature. These obstacles include: 1) the extensive genomic diversity associated with the HIV retrovirus, particularly with respect to the gene encoding the envelope protein, 2) the fact that the modes of viral transmission include virus-infected mononuclear cells, which pass the infecting virus to other cells in a covert form, as well as via free virus transmission, 3) existence of a latent form of the virus, 4) the ability of the retrovirus to "hide" in the central nervous system where blood cells and neutralizing agents carried by the blood cannot reach the

retrovirus, due to the blood-brain barrier and 5) the complexity and variation of the elaboration of the disease. The existence of these obstacles establish that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any vaccine or any immunization treatment or any therapeutic regimen on its face. In order to enable claims to drugs and their uses, either in vivo or in vitro data, or a combination of these can be used. However, the data must be such as to convince one of ordinary skill in the art that the claims are sufficiently enabled. When the claims are directed to humans adequate animal data would be acceptable in those instances wherein one of ordinary skill in the art would accept the correlation to humans. Thus in order to rely on animal data there must exist an art-recognized animal model for testing purposes. See In re Hartop, 311 F.2d 249, 135 USPQ 419 (CCPA 1962).

Yarchoan, et al. (J. Enz. Inh., 1992) state that while a number of agents have been found to block HIV binding to the target cell in vitro, these agents have generally not shown clear-cut evidence of clinical activity (abstract).moreover, Gait, et al. (TIBTECH 1995) discuss the problems associated with protein therapies for HIV and state that they suffer from problems of short serum half-life, poor bioavailability, and rapid clearance. Gait, et al. also teach that as these problems were overcome, other problems emerged such as sequestration of the drug by serum proteins, drug resistance, and uneven distribution throughout the body, and that since these types of problems are unpredictable, it remains necessary to take into account the pharmacological parameters (p. 437).

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986)and reiterated by the Court of Appeals in In re Wands, 8 USPQ 2d 1400 at 1404 (CAFC 1988). In the instant specification, it is determined that: 1) there are no working examples which suggest the desired results of inhibiting HIV infection *in vivo*, 2) the nature of the invention involved the complex and incompletely understood area of immunity to HIV, 3) the state of the prior art shows that prior treatment methods have been largely ineffective for the intended purpose, 4) the relative skill of those in the art is commonly recognized as quite high (post-doctoral level), and 5) the lack of predictability in the field to which the invention pertains is recognized in the art as evidenced by prior failures. In view of all of the above, it is determined that the specification is not commensurate in scope with the claimed invention.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

7. Claims 29, 31, 32, 41, and 45 rejected under 35 U.S.C. 102(e) as being anticipated by Berzofsky, et al. (U.S. Pat. No. 5,820,865). The claims are drawn to a method for directly inhibiting HIV entry into a cell comprising contacting the cell with a peptide comprising a specific sequence. It should be noted that the phrase "for directly inhibiting HIV entry into a cell" is viewed as intended and given little patentable weight. Berzofsky, et al. disclose a method for protecting cells from HIV comprising administering a composition which comprises a peptide having the claimed sequence to mice and restimulating the cells again by contacting the cells *in vitro* with the composition (cols. 3-4). The method of Berzofsky, et al. is the same as the claimed method. Therefore, Berzofsky, et al. anticipate the invention as claimed.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was

made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 30, 33-40, and 42-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berzofsky, et al. in view of Haynes, et al. (U.S. Pat. No. 5,013,548). The claims are drawn to a method for directly inhibiting HIV entry into a cell comprising contacting the cell with a peptide comprising a specific sequence. It should be noted that the phrase "for directly inhibiting HIV entry into a cell" is viewed as intended and given little patentable weight. The teachings of Berzofsky, et al. are described above. Berzofsky, et al. differ from the claimed invention by not specifically teaching peptides that have 8 amino acids or 24 amino acids and by not teaching peptides in the form of a multimer comprising a single chain of repeating units which can be linked via cysteines, spacer peptides, and a micelle. Haynes disclose methods of protecting animals against HIV comprising administering peptides which are similar to the claimed sequence and teach that the peptides inhibit syncytia formation (cols. 5-12 and Table 4). Haynes, et al. also teach that the peptides may contain one or more sequences from different isolates or the same isolate which can be linked via cysteines, may be conjugated to larger molecules, and may include a spacer. Therefore. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Berzofsky, et al. by employing peptides which contain one or more sequences from different isolates or the same isolate that can be linked via cysteines, may be conjugated to larger molecules, and may include a spacer as taught by Haynes, et al. Since both references teach peptides of varying length which comprise the claimed

RAFTIGK sequence it would have been obvious to one of ordinary skill in the art to produce peptides of varying length. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention because Haynes, et al. teach employing the peptides for preventing syncytia formation. Therefore, the invention as a whole is prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Examiner Brett Nelson, Art Unit 1648 and should be marked "OFFICIAL" for entry into prosecution history or "DRAFT" for consideration by the examiner without entry. The Art Unit 1648 FAX telephone number is (703)308-4426. FAX machines will be available to receive transmissions 24 hours a day. In compliance with 1096 OG 30, the filing date accorded to each OFFICIAL fax transmission will be determined by the FAX machine's stamped date found on the last page of the transmission, unless that date is a Saturday, Sunday or Federal Holiday with the District of Columbia, in which case the OFFICIAL date of receipt will be the next business day.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Brett Nelson whose telephone number is (703) 306-3219.

If the examiner can not be reached, inquiries can be directed to Supervisory Patent Examiner Chris Eisenschenk whose telephone number is (703) 308-0452.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

NELSON/bn
April 15, 1999

FRANK C. EISENSCHENK
PRIMARY EXAMINER
GROUP 1800
4/15/99